Hematopoietic Stem Cell Transplantation: An Overview

Tracy Robinson, RN MN, CON(C)
Clinical Nurse Specialist
Manitoba Blood and Marrow Transplant Program
CancerCare Manitoba
Complications:
- Acute and/or chronic GvHD
- Viral infections
- CMV, VZV, PCP, IP, HSV
- Bacterial infections
- VOD
- Secondaries tumors, cataracts, endocrine changes, QoL
- Mucositis

Supportive Therapy:
- Antibiotics
- Nutrition
- Antiemetic factors

BMT Process:
- Donor search or obtain autologous stem cells
- PBSC/BM harvests in ABMT
- eg: DHAP and GF and PBSC
- Collect & freeze gcsf

TIME LINE:
- 12 months
- 4 months
- 2 months
- 0 months
- 1 month
- 2 months
- 6 months
- 60 months

Disease State:
- Primary diagnosis and treatment
- Relapse and salvage therapy
- High-dose therapy
- Marrow failure
- Disease remission
- Disease recurrence
- Continuous complete remission (cure)
Objectives

- Definition
- Indications for transplant
- Types of transplant
- Stages of BMT
- Cell sources
- Complications of BMT
What is a HSCT

– Stem cell rescue
Hematopoiesis

Pluripotent Stem Cell → CFU-Blast

CFU-GEMM

CFU-Bl

BFU-E, CFU-Meg, CFU-GM

CFU-E, Megakaryocyte, CFU-G, CFU-M

Proplatelets, Reticulocyte, Red Blood Cell, Platelets, Neutrophil, Monocyte, Macrophage, Eosinophil, Basophil, Tissue Mast Cell, Plasma Cell, B Lymphocyte, T Lymphocyte, Natural Killer Cell

SCF, IL-3, IL-6, G-CSF, GM-CSF, IL-11, EPO, MGDF/TPD

©Amgen Inc. All rights reserved.
Purpose

• Eradicate malignancy
• Reset immune system
• Facilitate hematopoiesis
Diseases Treatable by HSCT

**Malignant**
- Leukemias and Lymphomas
- Myelodysplastic syndromes
- Multiple myeloma and other plasma cell disorders
- Solid tumors

**Non Malignant**
- Severe aplastic anemia and other marrow failure states
- Autoimmune diseases
- Inherited immune system disorders
- Inherited metabolic disorders
- Sickle cell disease and thalassemia
MBMT Program
Indication for Adult Transplants
1990-2012

Acute Myelogenous Leukemia
Acute Lymphoblastic Leukemia
Other Leukemia
Myelodysplastic Syndrome
Chronic Myelogenous Leukemia
Chronic Lymphocytic Leukemia/PLL
Non-Hodgkin's Lymphoma
Hodgkin's Lymphoma
Multiple Myeloma
Plasma Cell Disorder
Anemia/Hemoglobinopathy
Other Malignancy
Non-Malignant Disease
Transplants By Age Groups
1990-2012

- 0-17 years: 17%
- 18-40 years: 28%
- 41-55: 34%
- >56 years: 21%
Graft Types

• Autologous
• Allogeneic related (MRD)
• Allogeneic unrelated (MUD)
• MMUD → Haploidentical
• Syngeneic
MBMT Program
Total Transplants by Graft Type
1990-2013

- Autologous: 571
- Related Allogeneic: 320
- Unrelated Allogeneic: 252
- Syngeneic: 8

# of Transplants
Autologous HSCT

- Chemo to obtain disease control
- Stem cell collection

- Cells cryopreserved

- Admission to hospital for transplant/Prep regimen

- Cells reinfused
Autologous HSCT

• Advantages
  – Less risky (decreased TRM)
  – Available donor
  – No GVH

• Disadvantages
  – Disease recurrence
  – No GVL
  – Not suitable for all diseases
  – Cell collection
Allogeneic BMT

Recipient

High dose therapy
Immunosuppressive

Graft-versus-host disease prophylaxis

Donor
Allogeneic BMT

• Advantages
  – Uncontaminated cell sources
  – Used for bone marrow failure or malignancies
  – GVL effect

• Disadvantages
  – Riskier transplant
  – GHV effect
  – Cost
  – Donor availability
Haploidentical BMT

• Advantages
  – Donor accessibility

• Disadvantages
  – Riskier transplant
  – To be determined
Stages of the BMT Process

Phase 1: The Preparative Regimen (Conditioning Regimen) (Day-xxx to Day-1)
**GUIDELINES FOR PREPARATIVE REGIMENS (ADULT PATIENTS)**

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>AGE/KPS/PREBMT</th>
<th>AUTO</th>
<th>WELL MATCHED ALLO</th>
<th>PARTIALLY MATCHED ALLO</th>
<th>HAPLO Related Donor*</th>
<th>MISMATCHED ALLO or CORD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>&lt;50y and KPS&gt;90% or &gt;50y or KPS&lt;90%</td>
<td>N/A</td>
<td>CyTBI</td>
<td>CyTBI Thymo</td>
<td>Flu/Bu 12.8 + PT Cy</td>
<td>CyTBI Thymo FluBu 6.4Thymo</td>
</tr>
<tr>
<td>MYELOID (AML/MDS/MPN/CML)</td>
<td>&lt;50y and KPS&gt;90% or &gt;50y or KPS&lt;90%</td>
<td>Case specific</td>
<td>FluBu 12.8 Thymo</td>
<td>FluBu 6.4 Thymo</td>
<td>FluBu 12.8 Thymo</td>
<td>FluBu 6.4 Thymo</td>
</tr>
<tr>
<td>AA</td>
<td>N/A</td>
<td>N/A</td>
<td>FluCy120ATGAM or Thymo</td>
<td>FluCy120ATGAM or Thymo</td>
<td>FluCy120ATGAM or Thymo TBI 200</td>
<td>FluCy120ATGAM or Thymo TBI 200</td>
</tr>
<tr>
<td>CLL</td>
<td>N/A</td>
<td>N/A</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4 + PT Cy</td>
<td>FluBu 6.4 Thymo</td>
</tr>
<tr>
<td>NHL-aggressive</td>
<td>&lt;50y and KPS&gt;90% or &gt;50y or KPS&lt;90%</td>
<td>BEAM</td>
<td>CyTBI</td>
<td>CyTBI Thymo</td>
<td>FluBu 12.8 + PT Cy</td>
<td>CyTBI Thymo</td>
</tr>
<tr>
<td>NHL-indolent</td>
<td>N/A</td>
<td>BEAM</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4 + PT Cy</td>
<td>FluBu 6.4 Thymo TBI 200</td>
</tr>
<tr>
<td>HL</td>
<td>N/A</td>
<td>BEAM</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4 + PT Cy</td>
<td>FluBu 6.4 Thymo TBI 200</td>
</tr>
<tr>
<td>MM</td>
<td>N/A</td>
<td>Mel200</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4</td>
<td>FluBu 6.4 + PT Cy</td>
<td>FluBu 6.4 Thymo TBI 200</td>
</tr>
<tr>
<td>Germ Cell Tumor</td>
<td>N/A</td>
<td>CarboV P16</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* - All haploidentical transplants include post transplant cyclophosphamide, tacrolimus, and MMF for GVHD prophylaxis, and one of (1) 200 cGy TBI, (2) 400 cGy TBI, or (3) thiopeta
A CONTINUUM OF CONDITIONING REGIMENS

GENETIC DISPARITY

Immunosuppression

MUD

Matched sibling

Myelosuppression

CLL/AML/ALL

auto LCL

auto MM

AGGRESSIVENESS OF MALIGNANCY

AML/ALL

Flu Bu 6.4

F+Cy

Mel200

Mel/Etop

Mel/TBI

Cy + TBI

Flu Bu 12.8
Stages of the BMT Process

Phase 2: Hematopoietic Cell Infusion (Day 0)
MBMT Program
Allogeneic Cell Source
2011-2012

Adult Transplants

- PBSC: 87%
- BM: 9%
- CB: 4%

Pediatric Transplants

- PBSC: 35%
- BM: 56%
- CB: 9%
The Cells

– Bone Marrow
  • very rich
  • spongy soft tissue found inside larger bones
  • marrow removed in OR from iliac crests bilaterally with needles and syringes
The Cells

– Peripheral Blood Stem Cells (PBSC)
  • not as rich
  • requires growth factors (G-CSF)
  • apheresis procedure
  • no anesthesia
  • stem cells engraft faster
  • ↑GVHD
The Cells

– Umbilical Cord Blood Stem Cells
  • rich source
  • birth, collected, tissue-typed, processed and stored frozen
  • first done 1988
  • fixed amount cells»double cord (adult recipients)
  • no access to donor
  • unknown genetic disease
  • Expensive!
Graft Versus Host Disease Prophylaxis

- MRD/MUD 10/10
  - Immune suppression Day -2 and on
- Haplo
  - Post transplant cyclophosphamide
  - Day +7
Stages of the BMT Process

Phase 3: Recovery/Engraftment Period (Day +1 to +30)

Phase 4: Early Post BMT Period (Day +31- Day +100)
Early Complications

- Acute GVHD
- Bacterial & Viral Infection
- Stomatitis/Mucositis
- Nausea & Vomiting
- VOD/SOS
- Pneumonitis & Pulmonary Edema
- Dysrhythmia
- Renal insufficiency
- Recurrence of disease
Phases of Predictable Immune Suppression and Associated Opportunistic Infections

<table>
<thead>
<tr>
<th>Immune System Defects</th>
<th>Engraftment</th>
<th>Day 60</th>
<th>Day 90</th>
<th>Day 180</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphopenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transplant-related Factors Contributing to Infection</th>
<th>Engraftment</th>
<th>Day 60</th>
<th>Day 90</th>
<th>Day 180</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucositis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VOD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central line</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute GVHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic GVHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High Incidence Infections</th>
<th>Engraftment</th>
<th>Day 60</th>
<th>Day 90</th>
<th>Day 180</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VZV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early aspergillus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late aspergillus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viridans group streptococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facultative gram negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulase negative staphylococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low Incidence Infections</th>
<th>Engraftment</th>
<th>Day 60</th>
<th>Day 90</th>
<th>Day 180</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory and enteric viruses (episodic, endemic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encapsulated bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumocystis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epstein-Barr virus lymphoproliferative disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxoplasma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strongyloides Cryptosporidia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Stages of the BMT Process

• Phase 5: Late Post BMT Period (>Day +100)
Late Complications

- Chronic GVHD
- Infection
- Neurologic
- Ocular
- Dental
- Cardiac
- Pulmonary
- GI/GU
- Musculoskeletal
- Dermatologic
- Hepatic
- Endocrine
- Sexual
- Relapse
- Psychosocial
• The number of transplants performed annually worldwide is greater than 50,000
Causes of Death after Transplants Done in 2009-2010

**Unrelated Donor**
- Primary Disease (37%)
- Organ Failure (8%)
- Infection (18%)
- Other (18%)

**HLA-identical Sibling**
- Primary Disease (49%)
- GVHD (16%)
- Other (16%)
- Infection (13%)
- Organ Failure (5%)

**Autologous**
- Primary Disease (72%)
- New Malignancy (1%)
- Other (17%)
- Organ Failure (3%)
- Infection (7%)
So Why Do We Do This?
One-year Survival by Year of Transplant, Donor and Age, Worldwide, 1997-2010

- In any remission, Acute Leukemia, CML or MDS -
Thank You